

From the
INTERNATIONAL SEARCHING AUTHORITY

To:

see form PCT/ISA/220

PCT

WRITTEN OPINION OF THE
INTERNATIONAL SEARCHING AUTHORITY
(PCT Rule 43bis.1)

Date of mailing
(day/month/year) see form PCT/ISA/210 (second sheet)

Applicant's or agent's file reference
see form PCT/ISA/220

FOR FURTHER ACTION
See paragraph 2 below

International application No.
PCT/US2004/034169

International filing date (day/month/year)
15.10.2004

Priority date (day/month/year)
15.10.2003

International Patent Classification (IPC) or both national classification and IPC
C07D209/90, C07D209/94, C07D401/12, C07D405/12, C07D417/12, A61K31/403, A61P31/14

Applicant
CHIRON CORPORATION

1. This opinion contains indications relating to the following items:

- ☒ Box No. I Basis of the opinion
- ☒ Box No. II Priority
- ☒ Box No. III Non-establishment of opinion with regard to novelty, inventive step and industrial applicability
- ☐ Box No. IV Lack of unity of invention
- ☒ Box No. V Reasoned statement under Rule 43bis.1(a)(i) with regard to novelty, inventive step or industrial applicability; citations and explanations supporting such statement
- ☐ Box No. VI Certain documents cited
- ☒ Box No. VII Certain defects in the international application
- ☒ Box No. VIII Certain observations on the international application

2. **FURTHER ACTION**

If a demand for international preliminary examination is made, this opinion will usually be considered to be a written opinion of the International Preliminary Examining Authority ("IPEA"). However, this does not apply where the applicant chooses an Authority other than this one to be the IPEA and the chosen IPEA has notified the International Bureau under Rule 66.1bis(b) that written opinions of this International Searching Authority will not be so considered.

If this opinion is, as provided above, considered to be a written opinion of the IPEA, the applicant is invited to submit to the IPEA a written reply together, where appropriate, with amendments, before the expiration of three months from the date of mailing of Form PCT/ISA/220 or before the expiration of 22 months from the priority date, whichever expires later.

For further options, see Form PCT/ISA/220.

3. For further details, see notes to Form PCT/ISA/220.

Name and mailing address of the ISA:



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**WRITTEN OPINION OF THE
INTERNATIONAL SEARCHING AUTHORITY**International application No.
PCT/US2004/034169**1AP20 Rec'd PCT/PTO 14 APR 2006****Box No. I Basis of the opinion**

1. With regard to the **language**, this opinion has been established on the basis of the international application in the language in which it was filed, unless otherwise indicated under this item.
 - ☐ This opinion has been established on the basis of a translation from the original language into the following language , which is the language of a translation furnished for the purposes of international search (under Rules 12.3 and 23.1(b)).
2. With regard to any **nucleotide and/or amino acid sequence** disclosed in the international application and necessary to the claimed invention, this opinion has been established on the basis of:
 - a. type of material:
 - ☐ a sequence listing
 - ☐ table(s) related to the sequence listing
 - b. format of material:
 - ☐ in written format
 - ☐ in computer readable form
 - c. time of filing/furnishing:
 - ☐ contained in the international application as filed.
 - ☐ filed together with the international application in computer readable form.
 - ☐ furnished subsequently to this Authority for the purposes of search.
3. ☐ In addition, in the case that more than one version or copy of a sequence listing and/or table relating thereto has been filed or furnished, the required statements that the information in the subsequent or additional copies is identical to that in the application as filed or does not go beyond the application as filed, as appropriate, were furnished.
4. Additional comments:

**WRITTEN OPINION OF THE
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Box No. II Priority

1. ☒ The following document has not been furnished:

☒ copy of the earlier application whose priority has been claimed (Rule 43*bis*.1 and 66.7(a)).

☐ translation of the earlier application whose priority has been claimed (Rule 43*bis*.1 and 66.7(b)).

Consequently it has not been possible to consider the validity of the priority claim. This opinion has nevertheless been established on the assumption that the relevant date is the claimed priority date.

2. ☐ This opinion has been established as if no priority had been claimed due to the fact that the priority claim has been found invalid (Rules 43*bis*.1 and 64.1). Thus for the purposes of this opinion, the international filing date indicated above is considered to be the relevant date.

3. ☐ It has not been possible to consider the validity of the priority claim because a copy of the priority document was not available to the ISA at the time that the search was conducted (Rule 17.1). This opinion has nevertheless been established on the assumption that the relevant date is the claimed priority date.

4. Additional observations, if necessary:

**WRITTEN OPINION OF THE
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Box No. III Non-establishment of opinion with regard to novelty, inventive step and industrial applicability

The questions whether the claimed invention appears to be novel, to involve an inventive step (to be non obvious), or to be industrially applicable have not been examined in respect of:

- ☐ the entire international application,
- ☒ claims Nos. 1-59,89-104 (with respect to industrial applicability)

because:

- ☒ the said international application, or the said claims Nos. 1-59,89-104 relate to the following subject matter which does not require an international preliminary examination (*specify*):

see separate sheet

- ☐ the description, claims or drawings (*indicate particular elements below*) or said claims Nos. are so unclear that no meaningful opinion could be formed (*specify*):
- ☐ the claims, or said claims Nos. are so inadequately supported by the description that no meaningful opinion could be formed.
- ☐ no international search report has been established for the whole application or for said claims Nos.
- ☐ the nucleotide and/or amino acid sequence listing does not comply with the standard provided for in Annex C of the Administrative Instructions in that:
 - the written form ☐ has not been furnished
 - ☐ does not comply with the standard
 - the computer readable form ☐ has not been furnished
 - ☐ does not comply with the standard
- ☐ the tables related to the nucleotide and/or amino acid sequence listing, if in computer readable form only, do not comply with the technical requirements provided for in Annex C-*bis* of the Administrative Instructions.
- ☐ See separate sheet for further details

**WRITTEN OPINION OF THE
INTERNATIONAL SEARCHING AUTHORITY**

International application No.
PCT/US2004/034169

Box No. V Reasoned statement under Rule 43bis.1(a)(i) with regard to novelty, inventive step or industrial applicability; citations and explanations supporting such statement

1. Statement

Novelty (N)	Yes: Claims	1-104
	No: Claims	
Inventive step (IS)	Yes: Claims	1-104
	No: Claims	
Industrial applicability (IA)	Yes: Claims	60-88
	No: Claims	

2. Citations and explanations

see separate sheet

Box No. VII Certain defects in the international application

The following defects in the form or contents of the international application have been noted:

see separate sheet

Box No. VIII Certain observations on the international application

The following observations on the clarity of the claims, description, and drawings or on the question whether the claims are fully supported by the description, are made:

see separate sheet

**WRITTEN OPINION OF THE
INTERNATIONAL SEARCHING
AUTHORITY (SEPARATE SHEET)**

10/576045
14 APR 2006
PCT/US2004/034169

PCT/US2004/034169

Re Item III

Non-establishment of opinion with regard to novelty, inventive step and industrial applicability

Claims 1-59 and 89-104 relate to subject-matter considered by this Authority to be covered by the provisions of Rule 67.1(iv) PCT. Consequently, no opinion will be formulated with respect to the industrial applicability of the subject-matter of these claims (Article 34(4)(a)(I) PCT).

Re Item V

Reasoned statement with regard to novelty, inventive step or industrial applicability; citations and explanations supporting such statement

- D1: WO 01/49662 A (LIN HO SHEN ; LILLY CO ELI (US); RICHETT MICHAEL ENRICO (US)) 12 July 2001 (2001-07-12)
- D2: WO 01/51479 A (WARNER LAMBERT CO ; BOOTH RICHARD JOHN (US); JOSYULA VARA PRASAD VENKA) 19 July 2001 (2001-07-19)
- D3: WO 03/050119 A (DELLARIA JOSEPH F ; 3M INNOVATIVE PROPERTIES CO (US); MERRILL BRYON A) 19 June 2003 (2003-06-19)

Novelty

Document D1 discloses the use of tetrahydrocarbazoles, which structurally differ from the compounds of independent claims 1, 60 and 87, for the treatment of sPLA₂-induced diseases or conditions such as septic shock, adult respiratory distress syndrome, pancreatitis, trauma, bronchial asthma, allergic rhinitis and rheumatoid arthritis (see page 1, paragraph 1; page 2, paragraph 2; page 3, Formula (I); page 80, paragraph 3; Examples).

Document D2 discloses the use of carbazoles for the treatment of viral infections caused by viruses of the herpes family (see page 1, paragraph 1; page 2, paragraph 1, page 10, paragraph 2; Examples 432-446).

Lastly, document D3 discloses the use of imidazopyridine compounds for the treatment of viral infections such as hepatitis C or infections caused by viruses such as coronavirus (see page 1, line 9; page 2, Formula (I); page 28, lines 31, 32; Examples).

In view of this prior art, novelty has to be acknowledged for the subject-matter of present independent claims 1, 60, 87 and 90-102 and present dependent claims 2-59, 61-86, 88, 89, 103 and 104.

Inventive step

Document D3 has to be seen as closest prior art for the novel subject-matter, since it addresses the same problem, namely use and provision of compounds suitable for the treatment of hepatitis C or viral infections caused by coronavirus.

The distinguishing feature between the novel subject-matter and D3 is the particular basic chemical structure of the compounds of independent claims 1, 60 and 87 namely a tricyclic structure based on indol and a partially saturated carbocyclus.

In the absence of any evidence for an unexpected technical effect linked to this feature, the objective problem underlying the said novel subject-matter can merely be seen as use and provision of further compounds suitable for the treatment of hepatitis C or viral infections caused by coronavirus.

The claimed solution to this very general problem was the use of the particular compounds of present claim 1 and the provision of the particular compounds of present claims 60 and 87.

However, since this solution was not derivable from the prior art documents on file either read alone or in combination, the presence of inventive step has to be acknowledged for the novel subject-matter, even in the absence of a technical effect.

Industrial applicability

There is no doubt that the subject-matter of the present claims 60-88 is industrially applicable.

However, for the assessment of the present claims 1-59 and 89-104 on the question whether they are industrially applicable, no unified criteria exist in the PCT Contracting States. The patentability can also be dependent upon the formulation of the claims. The EPO, for example, does not recognize as industrially applicable the subject-matter of claims to the use of a compound in medical treatment, but may allow, however, claims to a

known compound for first use in medical treatment and the use of such a compound for the manufacture of a medicament for a new medical treatment.

Re Item VII

Certain defects in the international application

Independent claims 1 and 87 address different compounds. However, in both claims reference is made to a "compound of Formula I".

Where does R^3 come from in claims 86 and 87?

Re Item VIII

Certain observations on the international application

The breadth of claims 1-58, 60-84 and 86-89 should be such that it could be expected that all possibilities comprised would actually solve the problem underlying the application. Consequently, a claim should only include such possibilities (and their reasonable generalisations) which have been made credible in the specification. It appears thus that terms such as e.g. "alkyl", "perhaloalkyl", "alkoxyalkyl", "alkylsulfonyl", "alkylamino", "heterocycloalkyl", "aryl(alkyl)", and the like go far beyond what has actually been verified in the worked Examples on file. Moreover, a person skilled in the art cannot assume that all those possibilities which are e.g. comprised by a terminus such as "aryl" would be suitable in the sense of solving the present problem.

For the sake of clarity, indices such as e.g. " R^2 " or " R^3 " should always be superscript in order to better distinguish them from stoichiometric indices such as e.g. " CH_3 ".

For the sake of clarity, there should always be no more than 1 independent claim per category. However, the present set of claims comprises not less than 14(!) independent claims (1 and 90-102) directed to medical treatment.